Effects of dietary fat on cholesterol efflux and other cardiometabolic risk markers in humans

Valorization

Societal and economic relevance

Over the past decades, cardiovascular diseases (CVDs) have been the leading cause of death worldwide [1]. Currently, the number of CVD-related deaths is still growing. In 2016, approximately one third of all global deaths was due to CVDs. In addition, living with CVD or having a high CVD-risk lowers the health-related quality of life including physical and mental health [2]. The high number of CVDs also results in a high economic burden. In 2010, the global costs of CVDs added up to approximately 863 billion US dollars and it has been estimated that these costs will increase to 1044 billion US dollars in 2030 [3]. In Europe alone, the costs of CVDs are estimated to be 210 billion euros per year [4].

Coronary heart disease (CHD) is a common type of CVD and is often caused by atherosclerosis. Diet is one of the underlying causes for developing CHD and therefore dietary recommendations are needed to prevent CHD [1]. In order to develop these recommendations, dietary intervention studies are required that unravel the complex relationship between nutrition and CHD-risk. It is well-known that dietary saturated fat increases LDL-cholesterol, a risk factor for CHD, compared with unsaturated fats. It is therefore advised to keep the intake of saturated fat below 10% of daily energy [5]. However, saturated fat is an umbrella term for different saturated fatty acids that may exert different effects on CHD-risk factors. In fact, stearic acid (C18:0) does not increase LDL-cholesterol compared with carbohydrates [6] and lowers concentrations of LDL-cholesterol compared with other saturated fatty acids such as palmitic acid (C16:0) [7]. As palmitic acid and stearic acid are the most abundant saturated fatty acids in many Western diets, it is important that their potential differences in metabolic effects are considered when developing dietary guidelines for saturated fat intake. Based on the effect of stearic acid on LDL-cholesterol, the French Food Safety Agency (AFSSA) decided to exclude stearic acid from their dietary guidelines on atherogenic saturated fatty acids [8]. However, as CHD is a multifactorial disease, LDL-cholesterol is not the only underlying factor that contributes to the development of CHD. Although the effects of stearic acid compared with palmitic acid on LDL-cholesterol are well-known, the effects on other risk markers have been studied less extensively. Thus, more research is needed to draw conclusions about their effects on CHD-risk beyond LDL-cholesterol and get a comprehensive overview of their impact on cardiometabolic health. Therefore, we have focused in this dissertation on the effects of the most commonly consumed saturated fatty acids palmitic acid and stearic acid on conventional and emerging cardiometabolic risk factors. Ultimately, the findings of this research combined with findings of other scientists may provide underlying evidence for the development or revision of dietary guidelines. These guidelines will help the society to improve diet quality and will eventually contribute to the prevention of CHD and to public health in general.

Commercial relevance

As it is generally advised to reduce the intake of dietary saturated fatty acids, it is of great interest to the food industry to replace animal fats that are generally rich in saturated fatty acids with vegetable oils and fats rich in unsaturated fatty acids. In fact, the food industry nowadays heavily relies on the use of vegetable oils and fats for the production of processed foods, for example margarines and baked goods. However, for these food products, certain physical characteristics of the fats are required such as a specific melting behavior or solid fat content. To increase the suitability of vegetable oils and fats for the food industry, modification processes are used. For a long time, partial hydrogenation of vegetable oils was widely used. However, besides the formation of saturated fatty acids, also *trans* fatty acids were formed with partial hydrogenation. These industrially produced *trans* fatty acids are nowadays not allowed anymore as they have unfavorable effects on serum lipids and thereby increase the risk of developing CHD. An alternative to partial hydrogenation is interesterification, also known as the randomization of fats. Interesterification is a modification process that rearranges the fatty acids between and within triacylglycerol molecules resulting in new triacylglycerol species that have different physical characteristics, but without changing the overall fatty acid composition of the fat. Thus, in contrast to partial hydrogenation, no *trans* fatty acids are formed by interesterification [9]. However, even though no trans fatty acids are formed, it has been speculated that the position of the fatty acids within the triacylglycerol molecule determines its metabolic faith. More specifically, fatty acids at the *sn*-2 position are believed to remain attached to the glycerol backbone and end up in the liver where they will subsequently be incorporated into lipoproteins that enter the circulation. It may therefore be possible that interesterification of fats also affects cardiometabolic health. Vegetable fats and oils used for interesterification are often rich in palmitic acids and/or stearic acids. Normally, palmitic and stearic acids are mainly present at the outer *sn*-1 and *sn*-3 positions, but with interesterification the amount of these fatty acids at *sn*-2 increases. Thus, it is important that it is well-studied whether this position within the triacylglycerol molecules affects the metabolic faith of palmitic and/or stearic acids and thereby cardiometabolic health. As the existing literature on the effects of interesterification of palmitic acid- or stearic acid-rich fats is described in this dissertation, these results are also very relevant for the food industry. In addition, because stearic acid has a lowering effect on serum LDL-cholesterol compared to other saturated fatty acids, it has even been suggested that stearic acid-rich fats may be interesting for the production of functional foods

Environmental relevance

In the research described in this dissertation, we have predominantly studied effects of palm oil (rich in palmitic acids) and allanblackia oil (rich in stearic acids) on cardiometabolic health. These oils are both suitable for the production of interesterified fats. Palm oil, derived from the fruits of oil palm trees mainly found in Asia (i.e. Indonesia and Malaysia), is the most

commonly consumed vegetable oil. Palm oil consumption accounts for 30% of oil consumption worldwide. Almost half of the fatty acids in palm oil are palmitic acids. It has been estimated that around 75 million tonnes of palm oil will be consumed in 2019-2020 [10]. Although the production of palm oil is very efficient (one oil palm can produce up to 4000 liters of oil) and a good income source for the local producers, many people are concerned about the use of palm oil as its increased cultivation has among others resulted in negative effects on plant and animal biodiversity of some tropical forests, particularly in Malaysia. A large number of companies and organizations therefore work together to increase sustainability of the production of palm oil (also known as the Round Table on Sustainable Palm Oil). In the Netherlands, 90% of the palm oil used nowadays is sustainable. Nevertheless, due to the increasing world population and consumer society, it is still important to also use other vegetable oils and fats when possible. Allanblackia oil is derived from the fruit seeds of the Allanblackia tree commonly found at tropical forests in Africa (i.e. Tanzania and Ghana). The physical characteristics (solid at room temperature) of allanblackia oil, that are mainly due to its high stearic acid content (more than half of its fatty acids), make this oil very suitable to use as a structuring fat by the food industry [11]. Currently, allanblackia seeds are mainly harvested in the wild, but this wild harvesting alone will not meet long-term demands. Therefore, the 'Allanblackia Partnership' has been founded to increase the use and production of allanblackia oil in a sustainable way.

Translation into practice

Given that palmitic acid and stearic acid are the most abundant saturated fatty acids in many Western diets and that fats rich in palmitic and/or stearic acid are often used for interesterification by the food industry, it is important that we thoroughly understand their impact on metabolic health. Of course, this research alone is not enough to reconsider dietary guidelines for saturated fat nor to advise the food industry on which fats to use. Nevertheless, the reported findings of palmitic-acid and stearic-acid intakes on a broad selection of conventional and emerging cardiometabolic risk markers provide a foundation for future studies to confirm or refute these results. The question remains how all these findings translate into long-term metabolic health. Therefore, future research should also focus on functional cardiometabolic endpoints. The findings described within this dissertation were presented at several (inter)national congresses. In addition, the findings will be published in scientific journals and thus be publicly available for scientists as well as for policy makers and the food industry.

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